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Gene-Activated Bone Substitute Based on Octacalcium Phosphate and Doped with Magnesium Ions

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Abstract—This work is aimed at the optimization of the phase composition, surface morphology, and microstructure of matrices based on octacalcium phosphate (OCP) in order to increase the maximum dose and dosing accuracy of immobilized nucleic acids (NAs). It is determined that the modification of the scaffold with magnesium leads to a 1.4-fold increase in binding of plasmid DNA, which can further be used for the fabrication of medical products with the specified high concentration of biologically active NAs. Preliminary in vitro evaluation shows that the addition of magnesium to OCP regulates metabolic activity of HEK-293FT cell lines.

Keywords: bone substitute, gene-activated material, calcium phosphates, octacalcium phosphate, genes, nucleic acids

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INTRODUCTION

The annual number of patients who require reconstructive operations because of bone injuries is particularly large. In principle, a sufficiently effective treatment can be achieved using standard methods and materials (ordinary bone substitute, such as Osteomatriks (Konektbiofarm, Russia), Kolapol-KP-3 (NPO Polistom, Russia), Cerasorb (Curasan, Germany), Chronos (Synthes, Switzerland), and Trikafor (BioNova, Russia)) [1]. However, the desired results, namely, recovery of the initial quality of life, are not achieved for a large number of patients. This is caused by the fact that the number of cambial cells and biologically active substances in the defect zone, which induce reparative regeneration of tissues, is minimized and does not provide a complete histotypic recovery at large damage of tissues and organs; also, the presence of comorbidity and risk factors complicates the clinical setting [1]. Effective therapy in these cases can be provided only using materials and methods which affect the reparative regeneration of tissues, compensate for lost structures, replenish the cambial reserve, provide the factors that control the recovery process, and so on [2].

One of the routes for the solution of this problem is the employment of gene-activated bone substitute, which represent a particular class of medical products for bone grafting [3]. They are featured by the presence of genetic constructs, more specifically, biologically active nucleic acids (NAs), which carry the genes of therapeutic protein factors combined with the synthetic scaffold. To fabricate the latter, a rather large spectrum of materials are used today. In our opinion, the use of ceramic based on calcium phosphates (CPs), which represents a synthetic counterpart of bone tissue, is quite promising.

After implantation into the bone defect or the region of bone atrophy, genetic constructs are released from bone substitute, enter the cells of the recipient bed (immune competent cells, fibroblasts, and osteoblasts), and are expressed there for a particular time period to produce therapeutic protein, which is coded by the gene constructs [3, 4].

However, gene-activated materials based on CPs for tissue engineering possess some specific draw-